IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Ruiping LIU et al. Group Art Unit: 1624

Serial No.: 10/067,996 Examiner: Kahsay Habte

Filed: February 8, 2002

For: PHOSPHODIESTERASE 4 INHIBITORS

AMENDMENT AND SUBMISSION UNDER 37 CFR § 1.114.

Mail Stop-Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir: Further to the Request for Continued Examination filed herewith, please consider the following amendments.

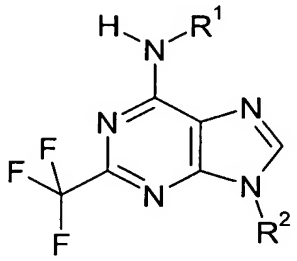
Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Remarks/Arguments begin on page 35 of this paper.

The following listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of Formula ~~I~~ I:



I

wherein,

R^1 is H,

alkyl having 1 to 5 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, or combinations thereof, and wherein a $-CH_2-$ group can be optionally replaced by -O-, -S-, or -NH-,

cycloalkyl having 3 to 6 carbon atoms, or

cycloalkylalkyl having 4 to 7 carbon ~~C~~ atoms; and

R^2 is alkyl having 1 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, cyano or combinations thereof, wherein one or more $-CH_2-$ groups is each independently optionally replaced by -O-, -S-, or -NH-, and wherein optionally one or more $-CH_2CH_2-$ groups is replaced in each case by –CH=CH- or -C≡C-,

alkyl ether having 3 to 12 carbon atoms,

cycloalkyl having 3 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano or combinations thereof,

cycloalkylalkyl having 4 to 12 carbon atoms ~~C atoms~~, which is unsubstituted or substituted one or more times by C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano, halogen, or combinations thereof,

aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

arylalkyl having 7 to 16 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heteroarylalkyl wherein the heteroaryl portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heteroaryl portion is unsubstituted or is substituted one or more times ~~in~~ by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heterocycle having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof ;

heterocycle-alkyl wherein the heterocycle portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heterocycle portion is nonarmoatic and is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof, or

carbocycle which is a nonaromatic, monocyclic or bicyclic, group having 5 to 14 carbon atoms, which is unsubstituted or is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof; ~~halogen,~~

~~aryl, C_{1-4}-alkyl, halogenated C_{1-4}-alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof;~~ and

pharmaceutically acceptable salts thereof,

with the provisos that:
(a) when R^1 is methyl, then R^2 is not arylalkyl, heteroarylalkyl, 2-(1,2,3,4-tetrahydro)quinolinyl-methyl, methyl or 2-butyl;
(b) when R^1 is cyclopropyl, R^2 is not 4-methylbenzyl;
(c) when R^1 is ethyl, then R^2 is not ethyl, 3-aminobenzyl, 2-thienylmethyl, 3-thienylmethyl, or 2-pyridylmethyl;
(d) when R^1 is cyclopropyl, then R^2 is not cyclopropylmethyl;
(e) when R^1 is H, then R^2 is not methyl, ethyl, benzyl, 4-methylbenzyl, or substituted tetrahydrofuranyl;
(f) when R^1 is methoxyethyl, then R^2 is not benzyl, 3-dimethylaminobenzyl, or 3-thienylmethyl;
(g) when R^1 is iso-butyl, then R^2 is not benzyl; and
(h) when R^1 is n-butyl, then R^2 is not n-butyl.

2. (Original): A compound according to claim 1, wherein when R^1 is methyl, R^2 is not arylalkyl, heteroarylalkyl, 2-(1,2,3,4-tetrahydro)quinolinyl-methyl or C_{1-5}-alkyl.

3. (Original): A compound according to claim 1, wherein R^1 is alkyl.

4. (Original): A compound according to claim 1, wherein R^1 is cycloalkyl.

5. (Original): A compound according to claim 1, wherein R^1 is cycloalkylalkyl.

6. (Original): A compound according to claim 1, wherein R^2 is alkyl.

7. (Original): A compound according to claim 1, wherein R^2 is alkyl ether.

8. (Original): A compound according to claim 1, wherein R^2 is cycloalkyl.

9. (Original): A compound according to claim 1, wherein R^2 is aryl.

10. (Original): A compound according to claim 1, wherein R^2 is arylalkyl.

11. (Original): A compound according to claim 1, wherein R^2 is heteroaryl.

12. (Original): A compound according to claim 1, wherein R^2 is heteroarylalkyl.

13. (Previously Presented): A compound according to claim 1, wherein R^2 is heterocycle.

14. (Previously Presented): A compound according to claim 1, wherein R^2 is heterocycle-alkyl.

15. (Previously Presented): A compound according to claim 1, wherein R^2 is carbocycle.

16. (Original): A compound according to claim 1, wherein R^1 is alkyl, substituted alkyl, cycloalkyl or cycloalkylalkyl.

17. (Original): A compound according to claim 6, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

18. (Original): A compound according to claim 7, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

19. (Original): A compound according to claim 8, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

20. (Original): A compound according to claim 9, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

21. (Original): A compound according to claim 10, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

22. (Original): A compound according to claim 11, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

23. (Original): A compound according to claim 12, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

24. (Original): A compound according to claim 13, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

25. (Original): A compound according to claim 14, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

26. (Original): A compound according to claim 15, wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

27. (Original): A compound according to claim 1, wherein R^1 is methyl, ethyl, isopropyl, 2-hydroxyethyl, cyclopropyl, cyclopentyl, or cyclopropylmethyl.

28. (Original): A compound according to claim 1, wherein R^1 is methyl, ethyl, cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

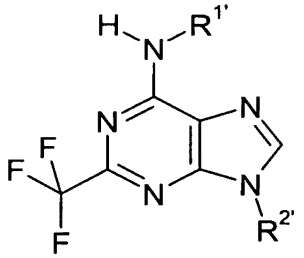
29. (Original): A compound according to claim 1, wherein R^1 is methyl, ethyl or cyclopropyl.

30. (Original): A compound according to claim 1, wherein R^2 is alkyl, arylalkyl, cycloalkyl, aryl, heteroaryl, heteroarylalkyl, or alkyl ether.

31. (Original): A compound according to claim 1, wherein R^2 is ethyl, isopropyl, butyl, tert-butyl, cyclopentyl, cyclohexyl, cycloheptyl, or arylalkyl which is unsubstituted or substituted one or more times by F, Cl, CN, CF_3, CH_3, C_2H_5, isopropyl, OCH_3, methylenedioxy, ethylenedioxy or combinations thereof.

32. (Original): A compound according to claim 1, wherein R^2 is substituted or unsubstituted benzyl, phenethyl or phenpropyl.

33. (Currently Amended): A compound of formula II



II

wherein

$R^{1'}$ is methyl, ethyl, or cyclopropyl; and

$R^{2'}$ is cycloalkyl having 3 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano or combinations thereof,

aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or

more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

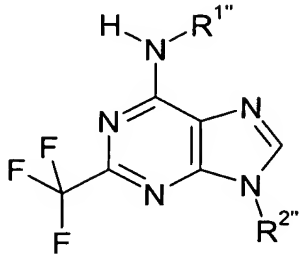
heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heterocycle having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof ~~(e.g., piperidinyl, imidazolinyl, imidazolidinyl, pyrrolinyl, pyrrolidinyl, morpholinyl, piperazinyl, and indolinyl)~~, or

carbocycle which is a nonaromatic, monocyclic or bicyclic, group having 5 to 14 carbon atoms, which is unsubstituted or is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof; and

pharmaceutically acceptable salts thereof.

34. (Previously Presented): A compound of Formula III:



III

wherein

$R^{1"}$ is methyl, ethyl, or cyclopropyl; and

$R^{2"}$ is phenyl,

phenyl which is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof, or

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, substituted heteroaryl having 5 to 10 ring atoms, in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4}-alkyl, C_{1-4}-alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino or combinations thereof,

or when R^1 is methyl or cyclopropyl R^2 can also be cycloalkyl having 3 to 12 carbon atoms; and

pharmaceutically acceptable salts thereof.

35. (Currently Amended): A compound according to claim 1, wherein said compound is selected from:

6-Cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine

6-Ethylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 6-difluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 3-difluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-propyl 2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3, 4-dimethoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3,4-methylenedioxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thiophenemethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-methylphenethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Methylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclohexyl-2-trifluoromethylpurine

6-Methylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentylmethyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-phenyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclobutyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-norboranane)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(1-indanyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-chlorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thienyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-cyclopentyloxy-4-methoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3, 4-dimethoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 6-dichloro-4-pyridylmethyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-methoxybenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-cyanophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2, 4-dimethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-nitrobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(6-methoxy-3-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-dimethylaminophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-aminophenyl)-2-trifluoromethylpurine
6-Methylamino-9-(2, 4-dimethoxy-5-pyrimidyl)-2-trifluoromethylpurine
6-Methylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-acetylphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-furanyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3, 4-methylenedioxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-ethoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3,4-dimethoxyphenyl)-2-trifluoromethylpurine; and

pharmaceutically acceptable salts thereof.

36. (Currently Amended): A compound according to claim 34, wherein said compound is selected from:

6-Cyclopropylamino-9-(2,3-difluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3,4-dimethoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Methylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclohexyl-2-trifluoromethylpurine

6-Methylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-phenyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclobutyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-norboranane)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-chlorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thienyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3, 4-dimethoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 6-dichloro-4-pyridylmethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-methoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-cyanophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-nitrobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-pyridyl)-2-trifluoromethylpurine

6-Methylamino-9-(2, 4-dimethoxy-5-pyrimidyl)-2-trifluoromethylpurine

6-Methylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-acetylphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-ethoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3,4-dimethoxyphenyl)-2-trifluoromethylpurine; and

pharmaceutically acceptable salts thereof.

37. (Cancelled):

38. (Previously Presented): A method according to claim 54, wherein said compound is administered in an amount of 0.01-100 mg/kg of body weight/day.

39. (Previously Presented): A method according to claim 54, wherein said patient is a human.

40. (Currently Amended): A method according to claim 54, wherein said compound is selected from:
6-Cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine;
6-Ethylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-fluorobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2, 6-difluorobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2, 3-difluorobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-propyl 2-trifluoromethylpurine
6-Cyclopropylamino-9-cyclopentyl-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3, 4-dimethoxybenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3,4-methylenedioxybenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-thiophenemethyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-methylphenethyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-cyclopropylmethyl-2-trifluoromethylpurine
6-Cyclopropylamino-9-cycloheptyl-2-trifluoromethylpurine
6-Methylamino-9-cyclopentyl-2-trifluoromethylpurine
6-Cyclopropylamino-9-cyclohexyl-2-trifluoromethylpurine
6-Methylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentylmethyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-phenyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclobutyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-norboranane)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(1-indanyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-chlorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-tolyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thienyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-cyclopentyloxy-4-methoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3, 4-dimethoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 6-dichloro-4-pyridylmethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-methoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-cyanophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 4-dimethoxyphenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-nitrobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(6-methoxy-3-pyridyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-pyridyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-pyridyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-dimethylaminophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-aminophenyl)-2-trifluoromethylpurine

6-Methylamino-9-(2, 4-dimethoxy-5-pyrimidyl)-2-trifluoromethylpurine

6-Methylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-acetylphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine

6-Methylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-furanyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3, 4-methylenedioxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-ethoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3,4-dimethoxyphenyl)-2-trifluoromethylpurine; and
pharmaceutically acceptable salts thereof.

41. (Original): A method according to claim 40, wherein said patient is a human.

42. (Original): A method according to claim 41, wherein said compound is administered in an amount of 0.01-100 mg/kg of body weight/day.

43. (Cancelled):

44. (Cancelled):

45. (Cancelled):

46. (Previously Presented): A method according to claim 57, wherein said patient is a human.

47. (Original): A method according to claim 46, wherein said patient is suffering from memory impairment.

48. (Previously Presented): A method according to claim 57, wherein said compound is administered in an amount of 0.01-100 mg/kg of body weight/day.

49. (Cancelled):

50. (Currently Amended): A method according to claim 57, wherein said compound is selected from:

6-Cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine

~~6-Methylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine~~

6-Ethylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 6-difluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2, 3-difluorobenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-propyl 2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3, 4-dimethoxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3,4-methylenedioxybenzyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thiophenemethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-methylphenethyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopropylmethyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Methylamino-9-cyclopentyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclohexyl-2-trifluoromethylpurine

6-Methylamino-9-cycloheptyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclopentylmethyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-phenyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-cyclobutyl-2-trifluoromethylpurine

6-Cyclopropylamino-9-(2-norboranane)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(1-indanyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-fluorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-chlorophenyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(4-tolyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-thienyl)-2-trifluoromethylpurine

6-Cyclopropylamino-9-(3-cyclopentyloxy-4-methoxybenzyl)-2-trifluoromethylpurine

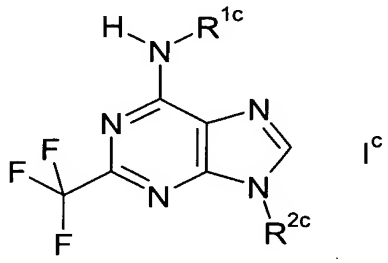
6-Cyclopropylamino-9-(3, 4-dimethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2, 6-dichloro-4-pyridylmethyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-methoxybenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-cyanophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2, 4-dimethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-nitrobenzyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(6-methoxy-3-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-pyridyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-dimethylaminophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-aminophenyl)-2-trifluoromethylpurine
6-Methylamino-9-(2, 4-dimethoxy-5-pyrimidyl)-2-trifluoromethylpurine
6-Methylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(4-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-acetylphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-methoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3-nitrophenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-furanyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(4-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(2-ethoxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3, 4-methylenedioxyphenyl)-2-trifluoromethylpurine
6-Cyclopropylamino-9-(3-ethoxyphenyl)-2-trifluoromethylpurine
6-Methylamino-9-(3,4-dimethoxyphenyl)-2-trifluoromethylpurine; and
pharmaceutically acceptable salts thereof.

51. (Previously Presented): A method according to claim 50, wherein said patient is a human.

52. (Cancelled):

53. (Cancelled):

54. (Currently Amended): A method for treating a patient having a disease involving decreased cAMP levels comprising administering to said patient an effective amount of a compound according to formula I^c:



I^c

wherein,

R^{1c} is H,

alkyl having 1 to 5 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, or combinations thereof, and wherein a $-CH_2-$ group can be optionally replaced by -O-, -S-, or -NH-,

cycloalkyl having 3 to 6 carbon atoms, or

cycloalkylalkyl having 4 to 7 carbon atoms ~~C atoms~~;

R^{2c} is alkyl having 1 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, cyano or combinations thereof, wherein one or

more -CH_2- groups is each independently optionally replaced by -O-, -S-, or -NH-, and wherein optionally one or more -CH_2CH_2- groups is replaced in each case by –CH=CH- or -C≡C-,

alkyl ether having 3 to 12 carbon atoms,

cycloalkyl having 3 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano or combinations thereof,

cycloalkylalkyl having 4 to 12 carbon atoms ~~C atoms~~, which is unsubstituted or substituted one or more times by C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano, halogen, or combinations thereof,

aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

arylalkyl having 7 to 16 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heteroarylalkyl wherein the heteroaryl portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heteroaryl portion is unsubstituted or is substituted one or more times in by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heterocycle having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof,

heterocycle-alkyl wherein the heterocycle portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heterocycle portion is nonarmoatic and is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof, or

carbocycle which is a nonaromatic, monocyclic or bicyclic, group having 5 to 14 carbon atoms, which is unsubstituted or is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof; and

pharmaceutically acceptable salts thereof,

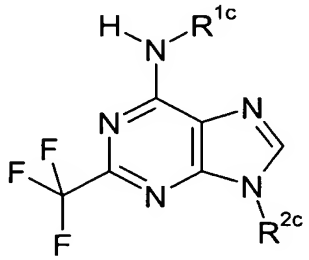
wherein when R^{1c} is methyl, then R^{2c} is not arylalkyl, methyl or 2-butyl, and when R^{1c} is H, then R^{2c} is not benzyl, and

with the proviso that said compound is not 6-methylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine.

55. (Cancelled):

56. (Previously Presented): A method according to claim 54, wherein:
(a) when R^{1c} is methyl, then R^{2c} is not arylalkyl, heteroarylalkyl, 2-(1,2,3,4-tetrahydro)quinolinyl-methyl, methyl or 2-butyl;
(b) when R^{1c} is cyclopropyl, R^{2c} is not 4-methylbenzyl;
(c) when R^{1c} is ethyl, then R^{2c} is not ethyl, 3-aminobenzyl, 2-thienylmethyl, 3-thienylmethyl, or 2-pyridylmethyl;
(d) when R^{1c} is cyclopropyl, then R^{2c} is not cyclopropylmethyl;
(e) when R^{1c} is H, then R^{2c} is not methyl, ethyl, benzyl, 4-methylbenzyl, or substituted tetrahydrofuranyl;
(f) when R^{1c} is methoxyethyl, then R^{2c} is not benzyl, 3-dimethylaminobenzyl, or 3-thienylmethyl;
(g) when R^{1c} is iso-butyl, then R^{2c} is not benzyl; and
(h) when R^{1c} is n-butyl, then R^{2c} is not n-butyl.

57. (Currently Amended): A method of inhibiting PDE4 enzyme activity in a patient comprising administering to said patient an effective amount of a compound according to formula I^c:



I^c

wherein,

R^{1c} is H,

alkyl having 1 to 5 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, or combinations thereof, and wherein a $-CH_2-$ group can be optionally replaced by -O-, -S-, or -NH-,

cycloalkyl having 3 to 6 carbon atoms, or

cycloalkylalkyl having 4 to 7 carbon atoms ~~C atoms~~;

R^{2c} is alkyl having 1 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, cyano or combinations thereof, wherein one or more $-CH_2-$ groups is each independently optionally replaced by -O-, -S-, or -NH-, and wherein optionally one or more $-CH_2CH_2-$ groups is replaced in each case by –CH=CH- or -C≡C-.

alkyl ether having 3 to 12 carbon atoms,

cycloalkyl having 3 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano or combinations thereof,

cycloalkylalkyl having 4 to 12 carbon atoms ~~C atoms~~, which is unsubstituted or substituted one or more times by C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano, halogen, or combinations thereof,

aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

arylalkyl having 7 to 16 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy,

cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heteroarylalkyl wherein the heteroaryl portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heteroaryl portion is unsubstituted or is substituted one or more times in by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heterocycle having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof,

heterocycle-alkyl wherein the heterocycle portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heterocycle portion is nonarmoatic and is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof,or

carbocycle which is a nonaromatic, monocyclic or bicyclic, group having 5 to 14 carbon atoms, which is unsubstituted or is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-

alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof; and

pharmaceutically acceptable salts thereof,

wherein when R^{1c} is methyl, then R^{2c} is not arylalkyl, methyl or 2-butyl, and when R^{1c} is H, then R^{2c} is not benzyl, and

with the proviso that said compound is not 6-methylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine.

58. (Cancelled):

59. (Previously Presented): A method according to claim 57, wherein:
(a) when R^{1c} is methyl, then R^{2c} is not arylalkyl, heteroarylalkyl, 2-(1,2,3,4-tetrahydro)quinolinyl-methyl, methyl or 2-butyl;
(b) when R^{1c} is cyclopropyl, R^{2c} is not 4-methylbenzyl;
(c) when R^{1c} is ethyl, then R^{2c} is not ethyl, 3-aminobenzyl, 2-thienylmethyl, 3-thienylmethyl, or 2-pyridylmethyl;
(d) when R^{1c} is cyclopropyl, then R^{2c} is not cyclopropylmethyl;
(e) when R^{1c} is H, then R^{2c} is not methyl, ethyl, benzyl, 4-methylbenzyl, or substituted tetrahydrofuranyl;
(f) when R^{1c} is methoxyethyl, then R^{2c} is not benzyl, 3-dimethylaminobenzyl, or 3-thienylmethyl;
(g) when R^{1c} is iso-butyl, then R^{2c} is not benzyl; and
(h) when R^{1c} is n-butyl, then R^{2c} is not n-butyl.

60. (Previously Presented): A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.

61. (Previously Presented): A composition according to claim 60, wherein said composition contains 0.1-50 mg of said compound.

62. (Cancelled):

63. (Cancelled):

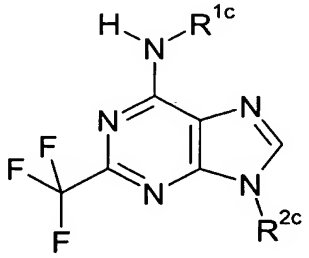
64. (Cancelled):

65. (Cancelled):

66. (Cancelled):

67. (Cancelled):

68. (Currently Amended): A method of treating a patient suffering from an allergic or inflammatory disease, resulting from decreased cyclic AMP levels, elevated phosphodiesterase 4 levels, or both, comprising administering to said patient an effective amount of a compound according to formula I^c:



I^c

wherein,

R^{1c} is H,

alkyl having 1 to 5 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, or combinations thereof, and wherein a $-CH_2-$ group can be optionally replaced by -O-, -S-, or -NH-,

cycloalkyl having 3 to 6 carbon atoms, or

cycloalkylalkyl having 4 to 7 carbon atoms ~~C-atoms~~;

R^{2c} is alkyl having 1 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, cyano or combinations thereof, wherein one or more $-CH_2-$ groups is each independently optionally replaced by -O-, -S-, or -NH-, and wherein optionally one or more $-CH_2CH_2-$ groups is replaced in each case by –CH=CH- or -C≡C-,

alkyl ether having 3 to 12 carbon atoms,

cycloalkyl having 3 to 12 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano or combinations thereof,

cycloalkylalkyl having 4 to 12 carbon atoms ~~C-atoms~~, which is unsubstituted or substituted one or more times by C_{1-4} alkyl, halogenated C_{1-4} alkyl, C_{1-4} alkoxy, cyano, halogen, or combinations thereof,

aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-

alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

arylalkyl having 7 to 16 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heteroarylalkyl wherein the heteroaryl portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heteroaryl portion is unsubstituted or is substituted one or more times in by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

heterocycle having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-

alkylamino, carboxy, alkoxycarbonyl, or combinations thereof,

heterocycle-alkyl wherein the heterocycle portion has 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom and the alkyl portion has 1 to 3 carbon atoms, the heterocycle portion is nonarmoatic and is unsubstituted or is substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, or combinations thereof,or

carbocycle which is a nonaromatic, monocyclic or bicyclic, group having 5 to 14 carbon atoms, which is unsubstituted or is substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof; and

pharmaceutically acceptable salts thereof,

wherein when R^{1c} is methyl, then R^{2c} is not arylalkyl, methyl or 2-butyl, and when R^{1c} is H, then R^{2c} is not benzyl, and

with the proviso that said compound is not 6-methylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine.

69. (Cancelled):

70. (Previously Presented): A method according to claim 68, wherein: (a) when R^{1c} is methyl, then R^{2c} is not arylalkyl, heteroarylalkyl, 2-(1,2,3,4-

tetrahydro)quinolinyl-methyl, methyl or 2-butyl;

(b) when R^{1c} is cyclopropyl, R^{2c} is not 4-methylbenzyl;

(c) when R^{1c} is ethyl, then R^{2c} is not ethyl, 3-aminobenzyl, 2-thienylmethyl, 3-thienylmethyl, or 2-pyridylmethyl;

(d) when R^{1c} is cyclopropyl, then R^{2c} is not cyclopropylmethyl;

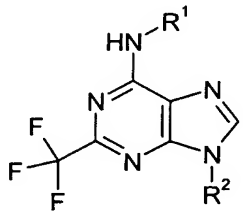
(e) when R^{1c} is H, then R^{2c} is not methyl, ethyl, benzyl, 4-methylbenzyl, or substituted tetrahydrofuranyl;

(f) when R^{1c} is methoxyethyl, then R^{2c} is not benzyl, 3-dimethylaminobenzyl, or 3-thienylmethyl;

(g) when R^{1c} is iso-butyl, then R^{2c} is not benzyl; and

(h) when R^{1c} is n-butyl, then R^{2c} is not n-butyl.

71. (Currently Amended): A process for preparing compounds of the formula IV



IV

wherein

R^1 is H,

alkyl having 1 to 5 carbon atoms, which is unsubstituted or substituted one or more times by halogen, hydroxy, or combinations thereof, and wherein a $-CH_2-$ group can be optionally replaced by -O-, -S-, or -NH-,

cycloalkyl having 3 to 6 carbon atoms, or

cycloalkylalkyl having 4 to 7 carbon atoms ~~C atoms~~; and

R^2 is aryl having 6 to 14 carbon atoms, which is unsubstituted or substituted one or more times by halogen, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, nitro, methylenedioxy, ethylenedioxy, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4}-hydroxyalkyl, C_{1-4}-hydroxyalkoxy, carboxy, cyano, hydroxamic acid, carboxamide, C_{2-4}-acyl, C_{2-4}-alkoxycarbonyl, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl, phenoxy, or combinations thereof,

heteroaryl having 5 to 10 ring atoms in which at least 1 ring atom is a heteroatom, which is unsubstituted or substituted one or more times by halogen, aryl, C_{1-4} alkyl, halogenated C_{1-4} alkyl, hydroxy, C_{1-4}-alkoxy, halogenated C_{1-4} alkoxy, cyano, trifluoromethyl, nitro, oxo, amino, C_{1-4}-alkylamino, di-C_{1-4}-alkylamino, carboxy, alkoxycarbonyl, hydroxamic acid, carboxamide, C_{1-4}-alkylthio, C_{1-4}-alkylsulphinyl, C_{1-4}-alkylsulphonyl,or combinations thereof,

said process comprising:
reacting 6-*N*-R^1-substituted adenine with an arylboronic acid or heteroarylboronic acid in the presence of trialkylamine wherein the alkyl portions each have 1 to 5 carbon atoms ~~of atoms~~, as a base, a copper catalyst, and a polar aprotic solvent, at a temperature of at least 50°C.

72. (Previously Presented): A compound according to claim 1, wherein R^2 is cycloalkylalkyl.

73. (Previously Presented): A compound according to claim 72 wherein R^1 is alkyl, cycloalkyl or cycloalkylalkyl.

74. (Previously Presented): A compound according to claim 1, wherein said compound is 6-cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof.

75. (Previously Presented): A method according to claim 54, wherein said compound is 6-cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof.

76. (Previously Presented): A method according to claim 57, wherein said compound is 6-cyclopropylamino-9-(2-methoxyphenyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof.

77. (Previously Presented): A compound according to claim 1, wherein said compound is 6-cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof

78. (Previously Presented): A method according to claim 54, wherein said compound 6-cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof.

79. (Previously Presented): A method according to claim 57, wherein said compound 6-cyclopropylamino-9-(2-fluorobenzyl)-2-trifluoromethylpurine, or a pharmaceutically acceptable salt thereof.

80. (Previously Presented): A compound according to claim 1, wherein R^1 is alkyl or cycloalkyl and R^2 is phenyl or heteroaryl, in each case substituted or unsubstituted.

81. (Previously Presented): A method according to claim 54, wherein R^1 is alkyl or cycloalkyl and R^2 is phenyl or heteroaryl, in each case substituted or unsubstituted.

82. (Previously Presented): A method according to claim 57, wherein R^1 is alkyl or cycloalkyl and R^2 is phenyl or heteroaryl, in each case substituted or unsubstituted.

REMARKS

Amendments

Claims 1, 33, 35, 36, 40 and 50 are amended to correct typographical errors. Claim 50 is also amended to delete the second compound, which is already excluded by the proviso clause in claim 57. Claims 54, 57, and 68 are amended to incorporate the recitations of claims 55, 58, and 69, respectively. In addition, claims 1, 33, 54, 57, 68, and 71 are amended to use the term "carbon atoms" consistently.

In view of the above remarks, allowance of the instant application is respectfully requested. The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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